Angiographic extent of coronary artery stenosis in patients with high and intermediate likelihood of unstable angina according to likelihood classification of American Heart Association

Amerikan Kalp Cemiyetinin olasılık sınıflamasına göre yüksek ve orta olasılıklı kararsız anjinalı hastalarda koroner arter tıkanıklığının anjiyografik yaygınlığı

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ABSTRACT

Objective: In accordance with the AHA/ACC clinical practice guideline, the likelihood of acute ischemia caused by coronary artery disease (CAD) is to be determined as high, intermediate, or low for all patients presenting with chest discomfort. This study was conducted to estimate extent of significant CAD in patients with high and intermediate likelihood of unstable angina (UA) according to "AHA likelihood classification"

Methods: Overall, 133 consecutive patients presented with symptoms or signs suggestive of UA, which was classified as of high or intermediate likelihood in Emergency Department (ED), and undergoing coronary angiography (CAG) within one week were enrolled into the study. The characteristics of the patients in either subgroup were compared in terms of the findings of the CAG.

Results: In patients with high likelihood of UA (n=89), CAG revealed that 62 had significant CAD, 7 - moderate CAD, 20 - mild CAD or normal coronary angiogram. In patients with intermediate likelihood of UA (n=19), CAG revealed that 2 patients had significant CAD, and 17 - mild CAD or normal coronary angiogram. The rate of significant CAD was significantly higher in patients with high likelihood (p<0.001, LR 23.97, 95% CI 4.21-90.43). The sensitivity and specificity of having at least one of high likelihood features for detecting significant CAD were found to be 96.8% and 38.6% respectively.

Conclusion: We suggest that the likelihood classification is useful for the triage of the UA patients in the ED. When supported with further studies, utilization of this classification will yield a high diagnostic accuracy in predicting or ruling out severe CAD in patients presenting with chest pain. *(Anadolu Kardiyol Derg 2007; 7: 287-91)*

Key words: Unstable angina, chest pain, coronary artery disease, emergency department, likelihood, classification, specificity and sensitivity

ÖZET

Amaç: AHA/ACC klinik uygulama kılavuzuna göre, göğüs ağrısı ile başvuran tüm hastaların koroner arter hastalığına bağlı akut iskemi olasılığı yüksek, orta ya da düşük olarak belirlenmelidir. Bu çalışma, AHA olasılık sınıflamasına göre, yüksek ya da orta olasılıklı kararsız anjinalı hastalardaki belirgin koroner arter hastalığının yaygınlığını tespit etmeyi hedeflemektedir.

Yöntemler: Kararsız anjinayı düşündüren semptom ve bulgularla başvuran, acil serviste yüksek ve orta olasılıklı sınıflandırılan ve 1 hafta içerisinde koroner anjiyografi yapılan ardışık 133 hasta çalışmaya alındı. Hastaların özellikleri alt gruplarına göre koroner anjiyografi bulguları ile karşılaştırıldı.

Bulgular: Yüksek olasılıklı hastalarda (n=89) koroner anjiyografi, 62 belirgin koroner arter hastalığı (KAH), 7 orta KAH, 20 hafif KAH ya da normal koroner arteri ortaya koydu. Orta olasılıklı hastalarda (n=19) koroner anjiyografi, 2 belirgin KAH, 17 hafif KAH ya da normal koroner arteri ortaya koydu. Belirgin koroner arter hastalığı, yüksek olasılıklı hastalarda daha belirgin sıklıkta bulundu (p<0.001, olasılıklar oranı 23.97, 95% güven aralığı 4.21-90.43). En az bir yüksek olasılık kriterine sahip olmanın, belirgin koroner arter hastalığını tespit etmedeki duyarlılığı ve seçiciliği, sırası ile %96.8 ve %38.6 bulundu.

Sonuç: Acil servislerde kararsız anjinalı hastaların triajında olasılık sınıflamasının kullanımının yararlı olacağını düşünüyoruz. Daha ileri çalışmalarla desteklediği takdirde, bu sınıflamanın kullanımı, göğüs ağrısı ile başvuran hastalarda ciddi koroner arter hastalığını önceden belirlemede ya da dışlamada yüksek tanısal doğruluk sağlayabilir. *(Anadolu Kardiyol Derg 2007; 7: 287-91)*

Anahtar kelimeler: Kararsız anjina, göğüs ağrısı, koroner arter hastalığı, acil servis, olasılık, sınıflama, seçicilik ve duyarlılık

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Introduction

Evaluating the chest pain patient is one of the greatest challenges facing the physicians despite major recent advances for diagnosing cardiac ischemia in both imaging technology and laboratory testing. In emergency departments (ED), identification of patients with acute coronary ischemia is extremely important step of ED evaluation of the patients with chest pain. Despite the use of new diagnostic tools, however, the physician still must take a thorough history and perform a careful physical examination, interpret the electrocardiogram (ECG) and order serial cardiac testing. Several clinical decision rules and strategies have been developed to aid in decision-making for patients presenting with signs or symptoms suggestive of acute coronary syndrome (ACS).

In 1994, the Agency for Health Care Policy and Research (AHCPR) published a definitive guideline for the diagnosis and management of unstable angina (UA). In a stepwise approach, the guideline stratifies patients into low, intermediate and high risk subgroups, according to the likelihood of coronary artery disease (CAD) and the short-term risk of acute myocardial infraction or death (1). The likelihood classification stratifies the patients according to angina characteristics, ECG, and CAD risk factors.

American Heart Association (AHA) and American College of Cardiology (ACC) have published several guidelines for the management of patients with UA and non-ST- elevation acute myocardial infraction. Some revisions on the original likelihood classification of Braunwald were done by AHA/ACC guidelines in 2000 and 2002. High troponin T, troponin I and creatine kinase-muscle band (CK-MB) level were added to the high likelihood criteria, and angina characteristics and ECG findings were revised. In accordance with 2002 ACC/AHA Guidelines for UA, determination of the likelihood of acute ischemia caused by CAD as high, intermediate, or low should be made in all patients with chest discomfort, and this is a class I recommendation (2). But, this recommendation has not been supported by strong evidence and stated as a level of evidence: C (level of evidence C: Only expert opinion, case studies, or standard-of-care). Stratification of patients with symptoms of unstable CAD according to risk likelihood is still recommended in 2005 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care (3).

Based on our literature search, there are no data on the diagnostic accuracy of the AHA likelihood classification in determination of the extent of CAD in patients with UA.

This study was conducted to determine extent of critical coronary artery disease in patients with high and intermediate likelihood of UA according to "AHA likelihood classification".

Methods

One hundred thirty-three consecutive patients were admitted to the Department of Emergency Medicine, Dokuz Eylül University hospital with diagnosis of UA within the study period between September 2002 and May 2003. Among them 108 (81.2%) patients were eligible for inclusion into the study and 25 patients were further excluded from the study because coronary angiography could not be performed. The exclusion criteria were also: ST-segment elevation indicative of acute myocardial infraction on baseline ECG and elevated CK-MB mass level.

All patients presented to ED with symptoms or signs suggestive of UA, were classified as having high (HL) or intermediate likelihood (IL) of UA, and had undergone coronary angiography (CAG) within one week after admission to the hospital. The patients were assigned to HL or IL subgroups for probability of significant CAD before CAG using the likelihood classification performed by emergency residents.

We used the original likelihood classification, which was recommended by AHCPR (2). We also added the high troponin I level into the classification as a new high likelihood criterion. The patients who had any of the following were classified within the HL group: definite angina; males ≥60 years or females ≥70 years of age; history of prior acute myocardial infraction or sudden death or other known history of CAD; variant angina; ST-segment elevation or depression ≥1mm; marked symmetrical T-wave inversion in multiple precordial leads; transient hemodynamic or ECG changes during pain; high troponin I level. The patients who had any of the following without high likelihood features were classified within the IL group: definite angina: males <60 years or females <70 years of age; probable angina: males ≥60 years or females ≥70 years of age; chest pain probably not angina in patients with diabetes; chest pain probably not angina in patients with at least two risk factors other than diabetes; extracardiac vascular disease; ST-segment depression 0.5-1 mm; T-wave inversion ≥1 mm in leads with dominant R waves; normal troponin I level.

Definition of Likelihood Features

Angina: The likelihood classification categorized the chest pain history of UA patients as definite angina, probable angina and probable not angina. However, there is no certain description of these clinical categories in the literature and in the likelihood classification (2-4). Therefore, we created a query, which had standard questions about nature of chest pain. This query was used to categorize chest pain as definite angina, probable angina and probable not angina (Table 1). If the patients described his/her pain with at least one of typical and atypical denominators, it was considered as probable angina. The patients who had defined his/her symptoms consistent with typical angina features it was considered as definite angina, while symptoms consistent with atypical angina features were considered probable not angina.

CAD risk factors: Smoking, diabetes mellitus, hyperlipidemia, hypertension and positive family history were considered as CAD risk factors.

Cardiac markers: At presentation and 12 hours after, troponin I and CK-MB mass determination were done. The patients with a high troponin I level (>1 ng/ml, range 0-1 ng/ml, testing performance within-run 3.1-7.1%, testing performance between-run 4.6-14.3%) were included in a HL group. The patients with high CK-MB mass level (>3.9 ng/ml, range 0-3.9 ng/ml, testing performance within-run 4.9-7.0%, testing performance between-run 7.0-8.3%) were excluded from the study since these patients were considered as having acute myocardial infraction. An immunometric assay (DPC, IMMULITE Turbo In-vitro Diagnostic Test Kit) was used by the institution during the study for assessment of the troponin and CK-MB mass levels.

Known history of CAD: The patients with a documented history of acute myocardial infraction, coronary artery bypass graft

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surgery or documented significant coronary artery stenosis by CAG were included in a HL group.

Coronary angiography: The degree of CAD as determined by CAG was classified as follows: 1) normal coronary angiogram; 2) mild CAD (<50% stenosis in one or more epicardial vessels); 3) moderate CAD (≥50% stenosis but <70% stenosis in one or more epicardial vessels); 4) significant single-vessel CAD (≥70% stenosis in one major epicardial vessel); 5) significant two-vessel CAD (≥70% stenosis in two major epicardial vessels); 6) significant three-vessel CAD (≥70% stenosis in all three major epicardial vessels); or 7) significant left main CAD (≥50% stenosis of the left main coronary artery).

Only stenoses of the graft vessels were searched for the evaluation of the patients with a coronary artery bypass grafts, not the native vessel stenosis. The cardiologists who evaluated CAG were blinded for patient's likelihood group whether high or intermediate.

Statistical analysis

Mann-Whitney test was performed comparison of continuous variables (age, cardiac markers) and Chi-Square test for categorical variables (risk factors of CAD, extent of CAD by coronary angiography, history of previous MI and history of coronary revascularization) using SPSS for Windows 11.0 version (Chicago, IL, USA) statistical computer software. Sensitivity (true positives/true positives + false negatives X 100) and specificity (true negative/true negative + false positive X 100) of high likelihood features for predicting significant CAD, and likelihood ratio with Chi-Square test were also calculated.

Results

Eighty-nine (82.4%) of 108 patients included into the study were classified as having HL, 19 patients were classified as of IL. Sixty-eight of the patients (63%) were male. Mean age of the patients was 64.37±11.07 (38-85) years. Demographic data and CAD risk factors are shown in Table 2.

In the HL group, 56 (62.9%) patients had documented CAD, 47 (52.8%) - high likelihood angina characteristics, 24 (27.0%) - high likelihood ECG features and 14 (15.7%) patients had high troponin I levels. There was no patient with variant angina in the HL group.

Angiographic results

Angiographic results of 108 patients enrolled in the study (Table 3) revealed that 64 (59.3%) patients had significant CAD, 7 (6.5%) - moderate CAD, and 37 (34.3%) patients had - mild CAD or normal coronary angiogram. While, 62 (69.6%) of patients with HL revealed significant CAD, only 2 (10.5%) of patients with IL revealed significant CAD. In patients with HL, significant coronary artery stenosis was more prevalent as compared to IL patients (p<0.001, LR 23.97, 95% CI 4.21 to 90.43).

The sensitivity and specificity of having at least one of HL features for detecting significant CAD were found as 96.8% and 38.6% respectively.

In the HL group, 45 (50.6%) patients had one criterion of high likelihood feature, 37 (41.6%) - two, and 7 (7.9%) patients had three criteria. While, in patients having one criterion of HL feature, significant CAD was detected in 57.8% of them, in

Table 1. Chest pain query form

Typical angina features
Retrosternal or epigastric discomfort described as crushing, squeezing, tightening or pressure-like.
Radiation to neck, back, jaw or arms.
Brought on by exertion and relieved by rest or nitroglycerin.
Dyspnea, nausea, vomiting or diaphoresis associated with pain.
Chest discomfort that is similar to a documented angina.
Atypical angina features
Pleuritic type chest pain (i.e., sharp or knife-like pain brought on by respiratory movements).
Primary or sole location of discomfort in the middle or lower abdominal region.
Pain reproduced with movement or palpation of the chest wall or arms.
Chest pain that lasts for many hours, or a few seconds.
Pain that may be localized at the tip of one finger.

Table 2. Demographic features and risk factors for CAD of the study patients

Parameters	Intermediate likelihood group (n = 19)	High likelihood group (n = 89)	p *
Age, years	59.36±10.23	65.43±11.00	0.02
Male, n (%)	8 (42.1)	60 (67.4)	NS
Diabetes mellitus, n (%)	9 (47.4)	28 (31.5)	NS
Hypertension, n (%)	14 (73.7)	52 (58.4)	NS
Hyperlipidemia, n (%)	7 (36.8)	53 (59.6)	NS
Smoking, n (%)	6 (31.6)	29 (32.6)	NS
Family history of CAD, n (%)	3 (15.8)	9 (10.1)	NS

*- p values significance by Mann-Whitney and Chi-square tests
CAD- coronary artery disease, NS - non-significant

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patients having two and three criteria of HL features, significant CAD was detected in 81.1% and 85.7% patients, respectively. High likelihood patients having two or three high likelihood features were more likely to demonstrate significant CAD as compared to patients having only one HL feature (p=0.014).

Discussion

Several computer-based decision protocols had been successfully used in United States and Europe for the appropriate triage of patients with acute coronary ischemia in the ED (4, 5). It was shown that computer-based decision programs such as an Acute Cardiac Ischemia Time-Insensitive Predictive Instrument (ACI-TIPI) is the most effective and most cost-effective method for this purpose. The use of ACI-TIPI led to appropriate triage of 97% of patients presenting with acute coronary ischemia and substantial reductions in admissions (5, 6). Nowadays, public access (via the website) computer programs have been studied to predict the existence of ACS in patients with chest pain at home (7). However, there is no standardized approach for the evaluation of chest pain patients in our country. Guideline-based, national, or institution-specific written protocols and decision algorithms should be established for triaging and managing of patients presenting to the ED with symptoms suggestive of ACS. In our national clinical practice, the application of "AHA likelihood classification" for the management and triage of patients presenting with chest pain is unknown.

Our study revealed that HL patients are significantly more likely to have angiographically confirmed critical coronary artery stenosis compared to the IL patients. The results suggest that "AHA likelihood classification" could discriminate the patients with critical coronary artery stenosis from those without in the ED environment.

Of all study patients, 64 of them showed significant CAD. Only two (3.1%) of them were classified in IL group, the others were classified in HL group. We found that HL features have a high sensitivity (96.8%) for detecting significant CAD. It seems that "AHA likelihood classification" is useful for predicting critical coronary artery stenosis before CAG. Using this classification for the triage

of patients presenting with chest pain suggestive of UA, can prevent inadvertent discharge of patients at high-risk for cardiovascular mortality or development adverse events in the ED.

Our study showed that patients with two or three HL features were more likely to have critical coronary artery stenosis compared to patients with only one high likelihood feature. We found that increasing numbers of HL features were associated with higher propensity to have critical coronary artery stenosis. We suggest that HL patients (especially in patients who have multiple high likelihood features), who presented to ED with a chest pain should be admitted to coronary care unit and evaluated with invasive strategies such as a CAG; because they have a higher frequency of critical coronary artery stenosis. Among patients with intermediate likelihood features, nearly 10% had critical coronary artery stenosis. Therefore, these patients may be evaluated with less invasive diagnostic modalities such as a treadmill stress test or dobutamine stress echocardiography in the ED survey. If they would not have evidence of myocardial ischemia in these tests, they should be discharged with follow-up.

Limitations of the study

Our study revealed that "AHA likelihood classification" helps us to triage of patients presenting with chest pain in ED. However, this study had limited number of patients therefore examining of "AHA likelihood classification" with our small study is not sufficient. This classification should be evaluated with larger clinical trials.

Conclusion

Our study demonstrates that patients with high likelihood of UA according to AHA classification more frequently have a critical coronary artery stenosis. The high likelihood features have a high sensitivity for detecting significant CAD. "AHA likelihood classification" should be applied by emergency physicians and cardiologists to all patients presenting with chest pain in ED. Further studies should be undertaken to validate the likelihood classification for the triage of patients with UA.

Table 3. Angiographic results of patients with high and moderate likelihood group.

Parameters	Intermediate likelihood patients (n = 19)	High likelihood patients (n = 89)	All patients (n = 108)
Significant CAD, n (%)	2 (10.5)	62 (69.7)	64 (59.3)
Significant left main CAD, n (%)	-	6 (6.7)	6 (5.5)
Significant three-vessel CAD, n (%)	1 (5.2)	8 (8.9)	9 (8.3)
Significant two-vessel CAD, n (%)	-	20 (22.4)	20 (18.5)
Significant single-vessel CAD, n (%)	1 (5.2)	28 (31.4)	29 (26.8)
Non significant CAD or normal coronary angiogram, n (%)	17 (89.5)	27 (30.3)	44 (40.7)
Moderate CAD, n (%)	-	7 (7.8)	7 (6.4)
Mild CAD, n (%)	7 (36.8)	13 (14.6)	20 (18.5)
Normal coronary angiogram, n (%)	10 (52.6)	7 (7.8)	17 (15.7)
CAD- coronary artery disease			

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